

## Original Contribution

### Prevalence of Smoking Assessed Biochemically in an Urban Public Hospital: A Rationale for Routine Cotinine Screening

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*Initially submitted March 31, 2009; accepted for publication June 24, 2009.*

Cotinine, a metabolite of nicotine, has been used to study tobacco smoke exposure in population studies, but the authors are unaware of its use to screen hospitalized patients. The authors measured serum cotinine levels in 948 patients admitted to an urban public hospital in San Francisco, California, between September 2005 and July 2006. On the basis of cotinine levels, they classified patients as active smokers (cotinine  $\geq 14$  ng/mL), recent smokers or significantly exposed to secondhand smoke (SHS) (0.5–13.9 ng/mL), lightly exposed to SHS (0.05–0.49 ng/mL), or unexposed ( $<0.05$  ng/mL). In contrast to the 13% prevalence of smoking in the general population of San Francisco, 40% of patients were active smokers; 15% were recent smokers or heavily exposed to SHS; 25% had low-level exposure to SHS; and 20% were unexposed. Active smoking or heavy SHS exposure was particularly high among African Americans (77%), the uninsured (65%), self-reported alcohol drinkers (77%), and illicit drug users (90%). Of people who denied smoking, 32% were found to have had significant exposure. If serum cotinine measurement became part of routine screening at urban public hospitals, cotinine levels would be abnormal in many patients and would provide objective evidence of tobacco smoke exposure, probably resulting in more intensive intervention to encourage patients to stop smoking and avoid SHS.

biological markers; cotinine; ethnic groups; hospitalization; smoking; tobacco; tobacco smoke pollution; vulnerable populations

Abbreviations: NHANES, National Health and Nutrition Examination Survey; SHS, secondhand smoke.

The prevalence of cigarette smoking in the United States has declined substantially in the past 50 years. Smoking prevalence averaged 40% in 1965, as compared with 20% in 2007 (1, 2). The decline in smoking has been greatest in better educated, more affluent smokers (2, 3). Smoking prevalence has declined to a much lower extent among less affluent, less well educated manual and service workers, people with mental illness or substance abuse disorders, and the homeless.

The state of California has been particularly successful in tobacco control; the prevalence of smoking among California adults is approximately 14% (<http://www.chis.ucla.edu/about.html>). Smoking prevalence in the city of San Francisco is even lower (about 12.5%). However, smoking behavior in a state or city as a whole does not reflect

smoking behavior in persons of lower economic status and in vulnerable populations.

Most patients admitted to hospitals are asked whether they smoke cigarettes. However, misreporting of smoking status is common, because of the negative social connotations of smoking and/or patients' concerns about revealing to health-care providers that they have failed to follow medical advice. Very few health-care providers ask patients about exposure to secondhand smoke (SHS), despite the well-established links between SHS exposure and cardiovascular disease, infectious diseases, and reproductive problems (4).

Tobacco use can be assessed biochemically. The most widely measured biomarker of tobacco use is cotinine, the proximate metabolite of nicotine. Cotinine has a much

longer half-life (16 hours) than does nicotine (2 hours), and cotinine is present in much higher concentrations in biologic fluids than nicotine (5, 6). Therefore, cotinine is a more sensitive marker of tobacco use than nicotine. Cotinine can be measured in blood, saliva, or urine and can detect smoking over the previous 3–5 days. Ultrasensitive assays for cotinine can detect exposure to SHS over the preceding few days as well (7).

While cotinine has been used in a number of population-based epidemiologic studies, such as the US National Health and Nutrition Examination Survey (NHANES) and the Health Survey of England (8–10), we are unaware of the use of cotinine to routinely screen hospitalized patients. Here we describe the results of routine screening of hospitalized patients at San Francisco General Hospital, an urban teaching hospital serving a largely uninsured and government-supported population. The specific aims of our study were 1) to assess the prevalence of tobacco exposure, including active and/or SHS exposure; 2) to compare prevalence rates with self-reported smoking; and 3) to examine smoke exposure prevalence as a function of demographic characteristics, the clinical service to which patients were admitted, insurance status, and alcohol and illicit drug use. Our results suggest that routine cotinine screening would be a high-yield test and might substantially improve tobacco control efforts among vulnerable populations.

## MATERIALS AND METHODS

### Study procedures

We identified all patients consecutively admitted to San Francisco General Hospital Medical Center between November 2005 and July 2006 who had medical record numbers ending in 3 or 7, who had had laboratory blood tests ordered within 24 hours of admission, and for whom an extra 1–2 mL of serum was available. If a subject was admitted more than once, only the first serum sample was used. Serum samples were refrigerated for 5–7 days and then frozen at  $-70^{\circ}\text{C}$  for later analysis. We retrospectively reviewed medical charts and collected data on each patient's age, sex, self-identified race/ethnicity, occupation, insurance status, self-reported smoking history, and admission diagnosis. At San Francisco General Hospital, all patients are supposed to have their smoking status recorded; there is a box on the admission nursing forms for recording smoking status. We also collected data on serum creatinine ( $n = 976$ ) and albumin ( $n = 415$ ) concentrations measured in the admission blood samples.

Because the study used blood that was to be discarded and because there was no direct patient contact, no consent from patients was required. Patients were not contacted in person for any information. The study was approved by the Committee on Human Research at the University of California, San Francisco.

### Analytical chemistry

Serum samples were analyzed for the concentration of cotinine in a 2-step process. Initially all samples were as-

sayed by gas chromatography with nitrogen phosphorous detection, which has a sensitivity of 5 ng/mL (11). Then those samples with concentrations less than 5 ng/mL were reassayed using a liquid chromatography-tandem mass spectrometry method with a sensitivity of 0.02 ng/mL (12).

### Data analysis

The prevalence of active cigarette smoking was examined using both a serum cotinine cutpoint of 14 ng/mL, based on the findings of Jarvis et al. (13) and as recommended by the Society for Research on Nicotine and Tobacco biochemical assessment working group (6), and using a cotinine cutpoint of 3 ng/mL, based on Benowitz et al.'s (14) recent analysis of a representative US population sample (NHANES data from 1999–2004). Recent smoking (e.g., when the patient stopped smoking a few days prior to admission because of sickness or lack of money for cigarettes), occasional smoking, and heavy SHS exposure cannot be distinguished biochemically. Thus, persons with these cotinine levels were combined into a group termed “recent smoking or SHS exposure,” which was defined as a cotinine concentration below the cutpoint for active smoking and at or above 0.5 ng/mL. A serum cotinine concentration of 0.5 ng/mL was selected as the lower level for significant SHS exposure, although disease may be caused by SHS resulting in cotinine levels as low as 0.05 ng/mL (12). Persons with serum cotinine concentrations of 0.05 ng/mL to 0.49 ng/mL were designated as having “low-level exposure.” Persons with cotinine levels less than 0.05 ng/mL were termed “unexposed.”

## RESULTS

Cotinine data were collected on 948 patients aged 18 years or older. Between September 2005 and July 2006, 10,873 patients were admitted to medical, surgical, and psychiatric wards at San Francisco General Hospital. A number of these patients were admitted 2 or more times, but data on multiple admissions were not available. We estimated that our sample represented approximately 10% of all hospitalized patients.

The study population included 62% men. The average age of the patients was 49 years (range, 18–93) (Table 1). The racial/ethnic distribution included 33% whites, 25% African Americans, 21% Latinos, 15% Asians, 0.5% Native Americans, and 4% persons of other or unknown race/ethnicity. The insurance status of the subjects included 53% with MediCal (Medicaid), 4% with Medicare, 28% with no insurance, 5% with private insurance, and 10% with another type of insurance or an unknown insurance status. Most patients (72%) were unemployed. Hospital clinical service upon admission was general medicine for 32% of subjects, trauma for 18%, cardiology for 12%, psychiatry for 9%, family practice for 8%, obstetrics and gynecology for 4%, and other for 17%.

Figure 1 shows the distribution of serum cotinine concentrations in the study population. Using the standard cotinine cutoff point of 14 ng/mL, 40% of adults were classified as

**Table 1.** Demographic Data on Adults<sup>a</sup> Admitted to San Francisco General Hospital between September 2005 and July 2006 (*n* = 948), San Francisco, California

Factor	No.	%
Sex		
Male	585	61.7
Female	363	38.3
Race/ethnicity		
Caucasian	317	33.4
African-American	239	25.2
Latino	203	21.4
Native American	5	0.5
Asian	145	15.3
Other	9	1.0
Unknown	30	3.2
Insurance coverage		
MediCal	504	53.2
Medicare	38	4.0
Private	48	5.1
None	268	28.3
Other/unknown	90	9.5
Cigarette smoking <sup>b</sup>		
Yes	331	34.9
No	295	31.1
Unknown	322	34.0
Alcohol consumption <sup>b</sup>		
Yes	296	31.2
No	331	34.9
Unknown	321	33.9
Illicit drug use <sup>b</sup>		
Yes	208	21.9
No	411	43.4
Unknown	329	34.7
Employment <sup>b</sup>		
Yes	166	17.5
No	678	71.5
Unknown	104	11.0

<sup>a</sup> Mean age = 49.4 years (range, 18–93).<sup>b</sup> Self-reported.

current smokers (Table 2). Using the newly proposed cotinine cutoff point of 3 ng/mL, 46% of adults could be classified as current smokers. Using a range of cotinine values between 0.5 ng/mL and 13.9 ng/mL, 15% of adults were classified as being recent smokers or SHS-exposed. Low-level exposure (0.05–0.49 ng/mL) was found in 25% of subjects. Only 20% of subjects were unexposed on the basis of a cutoff point of <0.05 ng/mL.

Table 2 presents numbers and percentages of patients in various demographic groups by smoke exposure category. For comparison of smoke exposures according to demographic characteristics, we combined the substantial expo-

sure groups of “current smoker” and “recent smoking/SHS exposure.” This combined group is referred to hereafter as persons with “significant smoke exposure.” Overall, 55% of adults fell into this category, including 63% of men and 42% of women. Significant smoke exposure differed by race/ethnicity; 80% of Native Americans, 77% of African Americans, 66% of whites, 35% of Latinos, and 22% of Asians were exposed. Significant smoke exposure differed by insurance status; 65% of the uninsured, 52% of MediCal recipients, 37% of Medicare recipients, and 29% of the privately insured were exposed. Unemployed patients had a 55% prevalence of significant smoke exposure, as compared with 61% of persons with an unknown employment status and 32% of the employed. The highest prevalence of significant smoke exposure was seen among patients in the psychiatry service (63%), followed by trauma (54%), medicine (50%), family practice (48%), and cardiology (47%).

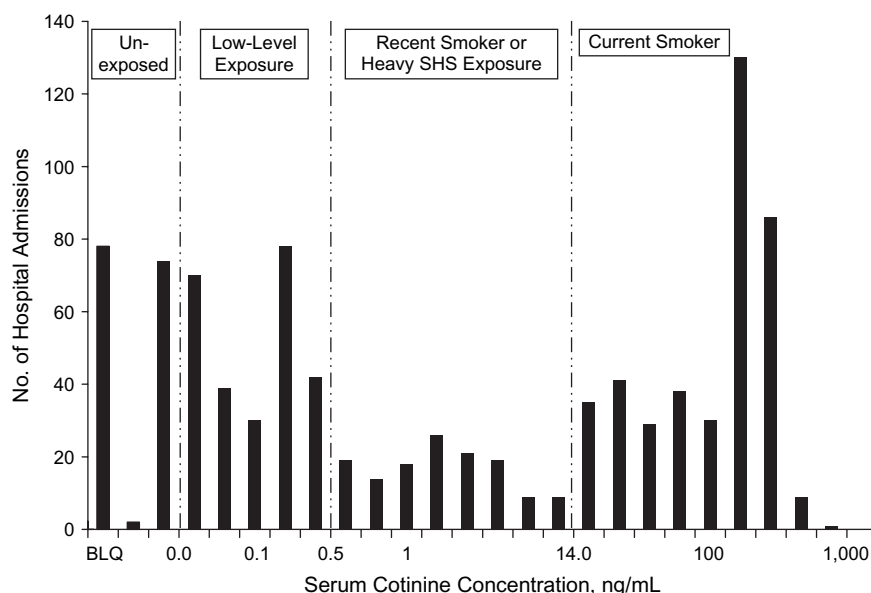
Smoking was self-reported by 35% of the subjects and nonsmoking by 31%; for 34%, smoking status was not recorded. Of those patients who reported smoking, 94% were confirmed to have been significantly exposed to tobacco smoke according to cotinine criteria. Of patients who reported not smoking, 32% were found to have significant exposure, and of those whose smoking status was unknown, 35% had significant exposure. Among patients with self-reported alcohol consumption, 77% had significant smoke exposure, as compared with 52% of those who denied alcohol consumption. Among patients who reported illicit drug use, 90% had substantial tobacco smoke exposure, as compared with 53% who denied illicit drug use.

Among patients who had their serum creatinine level measured, 26.4% had abnormally high values compared with age- and sex-based normal values used by the laboratory. Among patients who had their serum albumin level measured, 21% had abnormally low values compared with age-based normal values.

## DISCUSSION

In this paper, we have presented novel data on the prevalence of cigarette smoking and significant SHS exposure based on biochemical assessment of patients admitted to a major urban public hospital. In contrast to the relatively low prevalence in the general population of California (14%), significant tobacco smoke exposure in patients at San Francisco General Hospital was extraordinarily high, with 40% of patients found to be active smokers and 14% found to be recent smokers or heavily exposed passive smokers. These levels of exposure are similar to national smoking levels in the 1950s, when cigarette smoking was at its peak in the United States (2). An additional 25% of subjects had low-level exposure, leaving only 20% classified as unexposed.

Cigarette smoking is the most important preventable cause of premature disability and death in the United States and throughout the world. Reducing the prevalence of smoking has been a national priority since the publication of the 1964 Surgeon General’s Report on Smoking and Health, with considerable progress being made in reducing smoking



**Figure 1.** Serum cotinine concentrations in admission blood samples of adult patients admitted to San Francisco General Hospital, San Francisco, California, between September 2005 and July 2006. BLQ, below the limit of quantification; SHS, secondhand smoke.

prevalence in the general population since then (1, 3). However, as is the case for other disease risk factors, marked socioeconomic disparities are seen in smoking behaviors and the success of public health efforts. Smoking cessation has occurred to the greatest extent among better educated professionals (2, 3). Rates have remained high among less educated and unskilled workers, especially the unemployed and persons with mental health conditions, including alcohol and drug abuse (15). Among cigarette smokers, economically disadvantaged persons are also heavier smokers, as evidenced by higher saliva cotinine levels (10).

Urban public hospitals such as San Francisco General Hospital serve as a safety net, caring predominantly for people who have little or no health insurance, people with mental health and substance abuse disorders, and recent immigrants. Public hospitals frequently treat diseases caused by cigarette smoking, such as acute myocardial infarction and acute coronary syndrome, pneumonia, chronic obstructive lung disease, and lung cancer.

Our data on the demographic correlates of smoking are similar to national patterns (1). More men than women were smokers. The highest prevalence of smoking was seen in Native Americans, African Americans, and Caucasians, with lower prevalences in Asians and Latinos. Serum cotinine levels, reflecting daily nicotine exposure among smokers, were significantly lower in Asians and Latinos, which is consistent with general population data indicating that Asians and Latinos smoke fewer cigarettes per day than do Native Americans, Caucasians, and African Americans (16). Strong associations with smoking were seen for patients who were unemployed and had no insurance or had publicly financed insurance (MediCal). Self-reported alcohol (77%) and illicit drug (90%) use were also strongly associated with smoke exposure.

In other research, investigators have reported high rates of smoking in disadvantaged populations. For example, Lee et al. (17) screened residents of homeless shelters in Toronto, Canada, and found a 78% prevalence of cigarette smoking.

While one might expect that cigarette smoke exposure and therefore cotinine levels would be higher in a deprived population, the average cotinine level in our subjects was somewhat lower than that reported by O'Connor et al. (18) for a representative NHANES sample from 1999–2002. However, the cotinine levels were similar to those reported by Benowitz et al. (14) in another analysis of NHANES data. One difference between these studies was that the O'Connor study included adults aged 25 years or more (18), while the Benowitz study included adults aged 20 years or more (14). The present study included patients aged 18 years or more. Younger smokers are likely to be less heavy smokers. Furthermore, it is likely that cotinine levels in our samples were lower than usual for our subjects because of the time lapse between admission to a no-smoking hospital and the time of blood drawing and/or because of decreased smoking due to illness prior to hospital admission.

In accordance with current public health recommendations, San Francisco General Hospital staff routinely ask patients about their smoking status. As expected, in our study, most patients who reported smoking were confirmed biochemically to be smokers. Those who self-reported smoking and were not biochemically confirmed as smokers were probably those who had stopped smoking for at least a few days prior to admission because of illness or a lack of money to buy cigarettes. Considering an average half-life of 16 hours, cotinine levels could decline from smoker levels to nonsmoker levels in 2–4 days, depending on initial cotinine

**Table 2.** Tobacco Smoke Exposure Among Adults Admitted to San Francisco General Hospital between September 2005 and July 2006, as Determined by Serum Cotinine Concentration, San Francisco, California

Measure	Smoking Parameter and Serum Cotinine Level						Serum Cotinine Level Among Current Smokers, ng/mL	
	Unexposed or Low-Level Exposure (<0.49 ng/mL) (n = 428)		Recent Smoker or SHS-Exposed <sup>a</sup> (0.5–13.9 ng/mL) (n = 139)		Current Smoker <sup>a</sup> (≥14 ng/mL) (n = 381)		Mean	95% Confidence Interval
	No.	Row %	No.	Row %	No.	Row %		
Total	428	45.1	139	14.7	381	40.2	147.6	134.7, 160.6
Sex								
Male	216	36.9	95	16.2	274	46.8	151.0	138.1, 163.8
Female	212	58.4	44	12.1	107	29.5	139.1	117.9, 160.2
Race/ethnicity								
Caucasian	108	34.1	52	16.4	157	49.5	157.6	139.8, 175.5
African-American	55	23.0	40	16.7	144	60.3	165.2	146.6, 183.7
Latino	133	65.5	26	12.8	44	21.7	85.7	65.0, 106.4
Native American	1	20.0	1	20.0	3	60.0	83.0	–16.6, 130.5
Asian	113	77.9	13	9.0	19	13.1	101.2	72.0, 130.5
Other	7	77.8	1	11.1	1	11.1	167.7	— <sup>b</sup>
Unknown	11	36.7	6	20.0	13	43.3	123.3	75.7, 170.9
Smoking <sup>c</sup>								
Yes	17	5.1	39	11.8	275	83.1	158.1	144.7, 171.5
No	201	68.1	49	16.6	45	15.3	111.5	84.7, 138.4
Unknown	210	65.2	51	15.8	61	18.9	127.1	102.8, 151.4
Illicit drug use <sup>c</sup>								
Yes	19	9.1	38	18.3	151	72.6	147.7	129.0, 166.5
No	191	46.5	54	13.1	166	40.4	148.3	132.3, 164.3
Unknown	218	66.3	47	14.3	64	19.5	145.6	120.6, 170.6
Alcohol consumption <sup>c</sup>								
Yes	66	22.4	48	16.3	180	61.2	150.8	134.1, 167.5
No	160	48.0	41	12.3	132	39.6	145.4	127.4, 163.3
Unknown	202	62.9	50	15.6	69	21.5	137.0	107.4, 166.6
Insurance								
MediCal	240	47.6	74	14.7	190	37.7	137.1	122.6, 151.5
Medicare	24	63.2	6	15.8	8	21.1	206.8	122.0, 291.6
None	93	34.7	44	16.4	131	48.9	162.0	140.1, 183.1
Private	34	70.8	5	10.4	9	18.8	158.2	80.1, 236.4
Other/unknown	37	41.1	10	11.1	43	47.8	133.8	107.1, 160.1

Abbreviation: SHS, secondhand smoke.

<sup>a</sup> For comparison of smoke exposures according to demographic characteristics, the exposure groups of “recent smoker or SHS-exposed” and “current smoker” were combined. This combined group is referred to in the text as persons with “significant smoke exposure.”<sup>b</sup> Not applicable.<sup>c</sup> Self-reported.

levels. However, we also found that among patients who denied smoking, 15% were biochemically determined to be active smokers and 17% were found to be recent smokers or heavily exposed to SHS. Among patients for whom smoking status was not recorded (possibly related to an altered level of consciousness or uncooperativeness in the patient or failure of the nurse to ask), 19% were determined to be active smokers and 16% were determined to be recent smokers or heavily SHS-exposed. Thus, self-reports substantially underestimate the true prevalence of smoking in

this patient population, and biochemical testing is necessary to accurately identify persons with significant smoke exposure.

The selection of cotinine-based classifications of smoking status and the importance of SHS exposure warrant discussion. The cotinine cutoff point of 14 ng/mL was based on studies performed 20 years ago, when SHS exposure was high (9). This is a conservative cutoff point, meaning that virtually all persons with cotinine levels greater than or equal to 14 ng/mL are active tobacco users. Using this cutoff

point, 40% of our patients were active smokers. This is in contrast to recent US data in which the optimal cutpoint was determined to be 3 ng/mL in a representative sample of the US population evaluated between 1999 and 2004, a period when clean air regulations were widespread and SHS exposure was generally low (14). If we were to use the 3-ng/mL cotinine cutoff point, the prevalence of active smoking in our subjects would be even higher (46%). Cotinine is a metabolite of nicotine, and its presence is specific for nicotine intake. However, not everyone with elevated cotinine levels is necessarily a cigarette smoker. Nicotine can also be taken in from other forms of tobacco, such as smokeless tobacco, pipes, and cigars, and from nicotine-containing medications. However, in our experience, in the urban population of San Francisco there is relatively little use of forms of tobacco other than cigarettes and little use of nicotine medication, so the likely source of cotinine in the vast majority of our patients was exposure to nicotine from cigarette smoke.

Cotinine levels between 0.5 ng/mL and 13.9 ng/mL could represent a person who is an active smoker but has not smoked for several days or is a nondaily smoker. However, these levels are also consistent with significant SHS exposure. Significant SHS exposure is important because it is associated with increased risks of respiratory and cardiovascular disease and lung cancer (4). Very few health-care providers ask their patients about SHS exposure, and to our knowledge there have been no systematic studies of SHS exposure assessed biochemically in a general hospital population. Our data suggest that SHS exposure may be substantial among patients in a public hospital and that passive smoking should be part of the medical history recorded at admission. Finally, we found that 25% of our subjects had cotinine levels between 0.05 ng/mL and 0.49 ng/mL. While these persons are usually classified as nonsmokers, cotinine levels as low as 0.1 ng/mL secondary to SHS exposure appear to confer disease risk (12).

The question of the generalizability of our findings to all patients admitted to San Francisco General Hospital warrants discussion. We attempted to enroll patients consecutively on the basis of their medical record number, using a process designed to capture 20% of all admissions. However, the actual number of samples was approximately 10% of all admissions. The main reasons for our having fewer subjects than expected were lack of blood collection within 24 hours of admission and inadequate amounts of leftover serum for analysis. A disproportionate number of subjects without blood samples were admitted to the psychiatry service, which represents approximately 20% of admissions to San Francisco General Hospital but only 9% of subjects in our study. Since psychiatric patients had the highest rates of smoking, exclusion of some of these patients might have resulted in underestimation of smoking prevalence. On the other hand, one would presume that patients who did not have blood samples drawn within 24 hours were less acutely ill from a medical perspective than those who required immediate blood testing. It is possible that smoking would have been more prevalent in the more severely ill patients who had blood drawn early, resulting in overestimation of smoke exposure. Considering these limitations, with poten-

tial biases pointing in opposite directions, and considering that the number of subjects in our study was fairly large, we believe that our findings are representative of patients admitted with acute medical illness to an urban public hospital.

Based on the findings of our study, we recommend that measurement of blood cotinine concentration become a routine screening test for hospitalized patients. Routine screening typically includes a complete blood count, measurement of serum electrolyte and creatinine levels, and liver function tests. We found that 26% of patients had an abnormal serum creatinine value and 21% had an abnormal albumin value. By comparison, if cotinine measurement were a routine screening test, 40%–50% of patients at San Francisco General Hospital would have abnormal values. This is a far greater test yield than screening for creatinine or albumin level.

Routine cotinine screening of patients admitted to the hospital could have a great impact on patient care. Routine testing would provide unequivocal and objective evidence of smoke exposure. A positive test would signal health-care providers that there is a tobacco exposure problem. While a self-report of smoking history is useful in this regard, more than 30% of patients who deny smoking have significant tobacco smoke exposure when smoke exposure is examined objectively using serum cotinine levels. Furthermore, a finding of abnormal laboratory test values is a persistent reminder to health-care providers that there is a problem that needs to be addressed, similar to documentation of a high cholesterol level.

The methods of biochemical analysis used in this study—gas chromatography or liquid chromatography with tandem mass spectrometry—are technically demanding and expensive and would not be practical for routine use. However, automated immunoassays for cotinine that are adequately sensitive for the measurement of active smoking are available. These could be adapted for routine laboratory use. To the best of our knowledge, automated immunoassays with adequate sensitivity to quantify the low levels of cotinine that are observed after SHS exposure are not yet available.

In conclusion, our data provide biochemical evidence of an extraordinarily high prevalence of active and passive smoking in urban hospital patients, even in the state of California, where the prevalence of smoking is among the lowest of any state in the country. Self-reported information on smoking substantially underestimates the true prevalence of tobacco smoke exposure. Routine biochemical testing could identify greater numbers of smokers and would probably result in more intensive interventions to stop active smoking, eliminate SHS exposure, and reduce the health burden associated with smoking.

## ACKNOWLEDGMENTS

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This study was supported by the Flight Attendants Medical Research Institute and by US Public Health Service grant DA02277 from the National Institute on Drug Abuse.

The authors thank Lita Ramos and Duan Minjiang for performing the chemical analyses, Faith Allen for data management, and Marc Olmsted and Margaret Peng for editorial assistance.

Dr. Neal L. Benowitz is a consultant to several pharmaceutical companies that market medications to aid in smoking cessation and has served as a paid expert witness in litigation against tobacco companies. The other authors have no conflicts of interest to declare.

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